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Management of prolactinomas: a survey of physicians from the Middle East and North Africa

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Abstract
Background Prolactinomas are the commonest functional tumors of the pituitary gland. There are still controversies regarding medical therapy in specific clinical situations. Patients may be managed by different specialists in the Middle East and North Africa (MENA) region and no data exist on patterns of clinical management.
Objectives To ascertain the diagnostic and therapeutic approaches to prolactinomas among relevant professionals from the MENA region.
Methods An online survey of a large sample of physicians was conducted. The questionnaire covered various aspects of diagnosis and treatment of prolactinomas. 468 respondents were included; 36 % were endocrinologists; 49 % worked in public facilities and 81 % graduated more than 10 years. 40 and 30 % would have seen 1–5 and more than 5 suspected or confirmed prolactinomas over a 6 months period, respectively.
Results Regarding the diagnosis, 30 % of the respondents considered that prolactin levels <100 ng/ml exclude the presence of a prolactinoma. 21 % of respondents considered prolactin levels >250 ng/ml compatible with macroprolactinomas only, whereas others accepted this to be compatible also with microprolactinomas, macroprolactinaemia and drug-induced hyperprolactinemia (50, 42 and 36 % respectively). 71 % of respondents favored the screening for macroprolactin in asymptomatic individuals with hyperprolactinemia. Regarding the treatment, 84 % of respondents would treat microprolactinomas even in the absence of symptoms whereas 72 % of the respondents would treat microprolactinomas only if symptoms exist. 60 and 49 % of the respondents chose cabergoline as the drug of choice to treat macroprolactinomas and microprolactinomas respectively. Similar proportions had no preference of either cabergoline or bromocriptine as the best treatment

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for macroprolactinoma (27 %) and microprolactinomas (32 %). 46 and 75 % of respondents favored treatment withdrawal 2–3 years after prolactin normalization in patients with macroprolactinomas and microprolactinomas, respectively whereas 10 % of respondents withdraw treatment after menopause in either case. 94 % of respondents considered medical therapy as the primary treatment for microprolactinomas. In case of pregnancy, 49 % considered bromocriptine as the drug of choice for women who wish to become pregnant. 65 and 38 % of respondents advocated discontinuation of treatment with dopamine agonists in patients with microprolactinomas and macroprolactinomas, respectively. Finally, 48 % would allow breast-feeding without restriction, 28 % would restrict it to patients with microprolactinomas and 25 % would not recommend it for women with prolactinomas.
Conclusions This is the first study of the clinical management of prolactinomas in the MENA region. Some of the practices are not in line with the latest Endocrine and Pituitary Societies guidelines. These warrant further discussions of contemporary guidelines in regional forums.

Keywords Prolactin · Hyperprolactinemia · Pituitary tumors · MENA region

Introduction

Prolactinomas are the most frequent functional pituitary tumors and hyperprolactinemia is the most common disorder involving the hypothalamic-pituitary axis. Prolactinomas are conventionally classified according to their size as macroprolactinomas (>1 cm) or microprolactinomas (≤1 cm) [1, 2]. Untreated prolactinomas lead to galactorrhea, infertility, menstrual disorders, sexual dysfunction and bone loss as a result of hyperprolactinema and hypogonadism, as well as neurological and visual complications due to mass effect of larger tumors [1, 2]. Although the majority are microprolactinomas that mostly do not increase in size, more aggressive tumors may occur with mass effect, local invasion or rarely malignancy [1, 2].

Non-tumorous hyperprolactinemia and prolactinomas are amenable to medical therapy. Dopamine agonists (DAs), such as bromocriptine and cabergoline, are the treatment of choice for prolactinomas [4, 5]. Normalization of prolactin (PRL) levels, restoration of gonadal function and tumor shrinkage occur in most patients treated with these medications [1–4]. Nonetheless, challenging cases are not rare [6].

Despite the best practice recommendations from professional endocrine societies reflecting the evidence-base and expert opinion [4, 5], there are still several areas of controversies in the management (both diagnosis and treatment). Such controversies include the diagnostic cut off points of serum prolactin levels, choice of agents, the place of macroprolactin assays, initial management, duration of therapy, withdrawal of therapy, management before, during and after pregnancy, and the place of trans-sphenoidal surgery [3–7].

In the Middle East North Africa (MENA) region, patients with prolactinomas may be managed by different specialists such as endocrinologists, gynecologists, internists, and neurosurgeons. Also, management may be conducted under diverse settings of private, public and academic practices. No data pertaining to the patterns of clinical management of this condition exist from our region. Therefore, we have undertaken this investigation in an attempt to have a better understanding of practice patterns in the MENA region.

Materials and methods

Objectives

The aim was to evaluate how physicians from diverse specialties practicing in the MENA region approach the diagnosis and treatment of prolactinomas in general and in some clinical situations. These issues include different management strategies to macro as opposed to microprolactinomas, utility of macroprolactin assay, and management of prolactinomas during pregnancy and breast feeding.

Study design

A cross sectional electronic survey was conducted between May and November 2015. A commercial software (Survey Monkey, USA) was used. An invitation email with a link to the questionnaire was sent with full explanation of the rationale and method of participation. Five reminders were sent over the study period. In the original message academic purpose of the exercise and voluntary nature of the contribution, the unconditional right to decline participation and opt out from the data base permanently and the strict confidentiality in which data will be analyzed were all reiterated. Data were collected anonymously. No prior formal IRB approval is required in such quality assurance-type of exercises.

The questionnaire

The survey included 26 questions. 8 questions on the respondents' demographics and 18 questions constituted "*the prolactinoma questionnaire*" (Table 1) and one question was about ascertainment of access to resources.

Table 1 The "Prolactinoma Questionnaire": questions and [response options]

1. How would you interpret prolactin (PRL) levels <100 ng/ml? [A. They exclude the diagnosis of prolactinomas; B. They are rather indicative of pseudoprolactinomas and other causes of hyperprolactinemia] (Respondents could choose either, both or none)
2. In which conditions would you find PRL levels >250 ng/ml? [A. Only with macroprolactinomas; B. Also with microprolactinomas; C. Also in cases of macroprolactinemia; D. Also in cases of drug-induced hyperprolactinemia] (Respondents could choose either, both or none)
3. Would you favor the screening for macroprolactin? [Yes, Routinely; Only in asymptomatic patients]
4. When to treat microprolactinomas? [Always; Only in the presence of symptoms]
5. When to treat macroprolactinomas? [Always; Only in the presence of symptoms]
6. What is the drug of choice for MIC? [Bromocriptine (BCR); Cabergoline (CAB); either BCR or CAB]
7. What is the drug of choice for MAC? [Bromocriptine (BCR); Cabergoline (CAB); either BCR or CAB]
8. What is the maximum BCR daily dose do you prescribe? [5 mg; 7.5 mg; 10 mg; 15 mg; >15 mg]
9. What is the maximum CAB weekly dose do you prescribe? [2 mg; 2.5 mg; 3 mg; 3.5 mg; >3.5 mg]
10. How long should be treated patients with MIC who achieve normal PRL levels? [maintain treatment indefinitely; drug withdrawal after 2–3 years; drug withdrawal after menopause]
11. How long should be treated patients with MAC who achieve normal PRL levels? [maintain treatment indefinitely; drug withdrawal after 2–3 years; drug withdrawal after menopause]
12. Would you indicate surgery as primary therapy for microprolactinomas? [Yes/No]
13. What is the ideal drug for women who wish to become pregnant? [BCR; CAB; either BCR or CAB]
14. What is your approach for women with MIC who become pregnant in use of BCR? [discontinue BCR; change BCR to CAB; to maintain BCR or CAB]
15. What is your approach for women with MIC who become pregnant in use of CAB? [discontinue CAB; change CAB to BCR; maintain CAB]
16. What is your approach for women with MAC who become pregnant in use of BCR? [discontinue BCR; change BCR to CAB; maintain BCR or CAB]
17. What is your approach for women with MAC who become pregnant in use of CAB? [discontinue CAB; change CAB to BCR; maintain CAB]
18. Would you allow breast-feeding in women with prolactinomas? [No; only in cases of MIC; in cases of MIC or MAC]

For questions 1–2, respondents could choose as true either, both or none and for questions 4–18, only one answer was acceptable. Responding strategy was enforced by the survey software

PRL prolactin, *BCR* bromocriptine, *CAB* cabergoline, *MIC* microprolactinoma, *MAC* macroprolactinoma

The prolactinoma survey was analogous to the one used in previous study with similar objectives [8]. The original English language text was used as English is the language employed by most health care professions in the MENA region for professional and educational communication (other than when communicating with patients).

Study population

The MENA region is a newly recognized geopolitical and economic entity. There is no single master database for all endocrinologists. A large convenience sample included practicing physicians who were identified on academic databases of health-related bodies, professional groups and recent continuous professional development (CPD) events and/or by virtue of their contribution to the medical literature in the subject. Primary inclusion criteria were being a medically qualified physician practicing in the MENA region. Respondents were asked to define themselves in terms of specialties, age group, duration and volume of practice etc. Only respondents practicing in the MENA region were included in the analysis.

Statistical analysis

Results are adjusted as percentages to take account of the missing responses. Comparisons were tested using *t*-tailed Fisher's exact test when appropriate. $P < 0.05$ was considered statistically significant.

Results

Respondents' professional and practice profiles

Responses of 468 participants were eligible for inclusion in the study. Respondents were from United Arab Emirates (238), Saudi Arabia (50), Qatar (27), Egypt (26), Libya [20], Kuwait [20], Iraq [14], Oman [11] and Pakistan [11]. Smaller numbers [1–6] came from other countries in the

region. Other countries were not represented due to lack of respondents and not due to deliberate exclusion. No data collection was possible on non-respondents. Professional and clinical practice profiles and reported access to resources related to management of pituitary disease are different between endocrinologists and not endocrinologists (Table 2). It is anecdotally noticeable that access to investigative and therapeutic facilities vary between and within countries of the region. However, difference in representation from different countries prevented making any meaningful country-wise examination of the data.

Diagnostic evaluation

Prolactin levels <100 ng/ml was considered by 28 % of the respondents to exclude the diagnosis of prolactinoma and 68 % of them stated that such level is rather indicative of non-tumorous causes of hyperprolactinemia. However 2 and 16 respondents chose both options or made no choice respectively. Prolactin levels >250 ng/ml was considered by 21 % of respondents to be found exclusively in patients with macroprolactinomas. The remainder thought that such levels could also be found in patients other conditions (Fig. 1). The interpretation of these two cut off levels were different by endocrinologists and non-endocrinologists (Fig. 1). Less respondents favored the routine screening for macroprolactin (29 %) rather than only in asymptomatic patients (71 %). Endocrinologists and non-endocrinologists were not significantly different in rates of routine requesting of macroprolactin (27 vs. 29 %) nor in asymptomatic patients (73 vs. 71 %) ($P = 0.07$).

Treatment of prolactinomas

In general, 72 and 84 % of the respondents would use DAs in asymptomatic micro and macroprolactinomas respectively. The remaining respondents (28 and 16 %) would only treat patients with micro and macroprolactinomas respectively if they have symptoms. The responses pertaining to decisions to treat, durations of treatment and choices of medication for all responses and by endocrinologist and non-endocrinologists separately for both cases of micro- and macroprolactinomas are presented in Table 3 and Fig. 2. Differences were observed in approaches to management of microprolactinomas compared to macroprolactinomas (Table 3; Fig. 2). Differences were also observed between endocrinologists and non-endocrinologists in various aspects of management (Table 3). Compared to all respondents, endocrinologists recommended drug withdrawal more often for both micro-and macroprolactinomas (Table 3). The maximum dose of cabergoline was diverse ranging between 2 and 3.5 mg/week whereas that of bromocriptine varied from 7.5 to 15 mg/day. Similar pattern was observed when only endocrinologists were included. 6 % of respondents indicated surgery as primary therapy for microprolactinomas; marginally less so (4 %) among endocrinologists (Table 3).

Prolactinomas during pregnancy and breastfeeding

More respondents chose bromocriptine, instead of cabergoline, as the drug of choice for women who wish to become pregnant (49 vs. 30 %). Endocrinologists and non-endocrinologists differed in their DA of choices (endocrinologists: 55 vs. 22 %; non-endocrinologists: 45 vs. 35 %; $P < 0.01$) for bromocriptine and cabergoline respectively. 20–23 % expressed no particular preference. The various courses of action taken by physicians when a woman with prolactinoma on DA therapy become pregnant are depicted in Fig. 3. In addition, 78–85 and 33–38 % of endocrinologists would discontinue DA treatment in pregnant women with microprolactinomas and macroprolactinomas respectively. Regarding breast feeding, 46 % of all respondents unconditionally allow breastfeeding for women with either macro or microprolactinomas, 28 % would allow it in cases of microprolactinomas only and 25 % would not recommend breast-feeding for women with prolactinomas at all. Among the endocrinologists, 50 % considered it safe for all patients, 30 % allowed it for microprolactinomas and 20 % did not allow breast-feeding at all. No differences were detected between endocrinologists and other physicians.

MENA survey versus the Brazilian survey

The salient responses of endocrinologists from the present survey were compared to the survey from Brazil [8]. Data on diagnostic evaluation, management in general and management before and during pregnancy are summarized in Table 4.

Discussion

Diagnosis of prolactinoma is often straightforward and also the treatment strategy has been well defined in recent guidelines [4, 5]. However, several challenging issues persist in their management that have been highlighted recently [6, 7]. The differential diagnosis of a large pituitary tumor with moderately elevated prolactin concentrations sometimes can be difficult, and prolonged treatment with a dopamine agonist may be inappropriate when the diagnosis of a prolactinoma is not sufficiently well substantiated. In addition, timely withdrawal of dopamine agonist treatment and the indications of trans-sphenoidal surgery are still

Table 2 Professional and practice profile characteristics of the respondents

Characteristics	Details	All	Endocrinologists	Non-endocrinologists
Specialty[a]	Endocrinologist	168	168 (36.1 %)	–
	Internist (endocrine interest)	83	–	83 (18 %)
	General internist	42	–	42 (9 %)
	Gynecologist	30	–	30 (6 %)
	Neurosurgeon	12	–	12 (3 %)
	Primary care physician	80	–	80 (17 %
	Others	51	–	51 (11 %)
Grade	Consultant (attending)	206 (44 %)	121 (72 %)	85 (29 %)
	Specialist (sub-consultant)	183 (39 %)	45 (27 %)	138 (46 %)
	All other grades	77 (17 %)	2 (1 %)	75 (25 %)
Practice type	Academic[b]	117 (25 %)	54 (32 %)	63 (21 %)
	Clinical: private sector	119 (26 %)	52 (31 %)	67 (23 %)
	Clinical: public sector	226 (49 %)	62 (37 %)	164 (56 %)
Clinical experience[c]	Longer than 20 years	185 (40 %)	74 (44 %)	111 (38 %)
	Between 10 and 20 years	189 (41 %)	62 (37 %)	127 (43 %)
	Less than 10 years	89 (19 %)	31 (19 %)	58 (20 %)
Number of patients with prolactinoma[d]	None	140 (30 %)	9 (6 %)	130 (44 %)
	1–5 patients	187 (40 %)	67 (40 %)	119 (40 %)
	5–10 patients	74 (16 %)	49 (29 %)	25 (9 %)
	10–15 patients	36 (8 %)	26 (16 %)	10 (34 %
	More than 15 patients	27 (6 %)	16 (10 %)	11 (4 %)
Access to resources	Endocrinologist	–	–	81 %
	Pituitary surgeon	46.3 %	64 %	36 %
	Conventional radiotherapy	37.7 %	49 %	31 %
	Stereotactic radiotherapy	18.0 %	30 %	11 %
	Hormonal measurements[a]	64.0 %	72 %	58 %
	Cabergoline	73.8 %	91 %	64 %
	Bromocriptine	75.6 %	89.6 %	68 %
	Neuroradiology–MRI	64.5 %	82 %	55 %
	Neuroendocrine MDT	13.1 %	21 %	8 %
	"Best practice guidelines"	36.1 %	40 %	34 %

Data for all of the 468 respondents, endocrinologists only (168) and non-endocrinologists only (298) are presented separately. Data are given as number and/or (%) as deemed appropriate

MDT multidisciplinary team

[a] Best fitting description

[b] Mainly teaching/research

[c] Since graduation

[d] Seen in the previous 6 months

matters of debate. Last but not least, the management of resistant or aggressive prolactinomas remains a challenge for clinicians, especially in young patients [6, 7].

There are no data on management of prolactinoma in the MENA region other than case reports or small case series. These case reports cannot reflect the general trends in clinical practice in the region. This is the first study of the clinical management of prolactinoma from the MENA region. We aimed to assess the practice trends via ascertaining knowledge, and attitude of physicians. The survey established some baseline information for future reference and emphasizes the need for continuous medical education planning and perhaps inspires more regional research in this and similar areas.

Many practicing endocrinologists in the MENA region do share similar past training backgrounds (mostly British and French) and current professional affiliations (mostly North American and European). Training to become an endocrinologist is variable in various parts but majority of practicing endocrinologists involved in the current survey

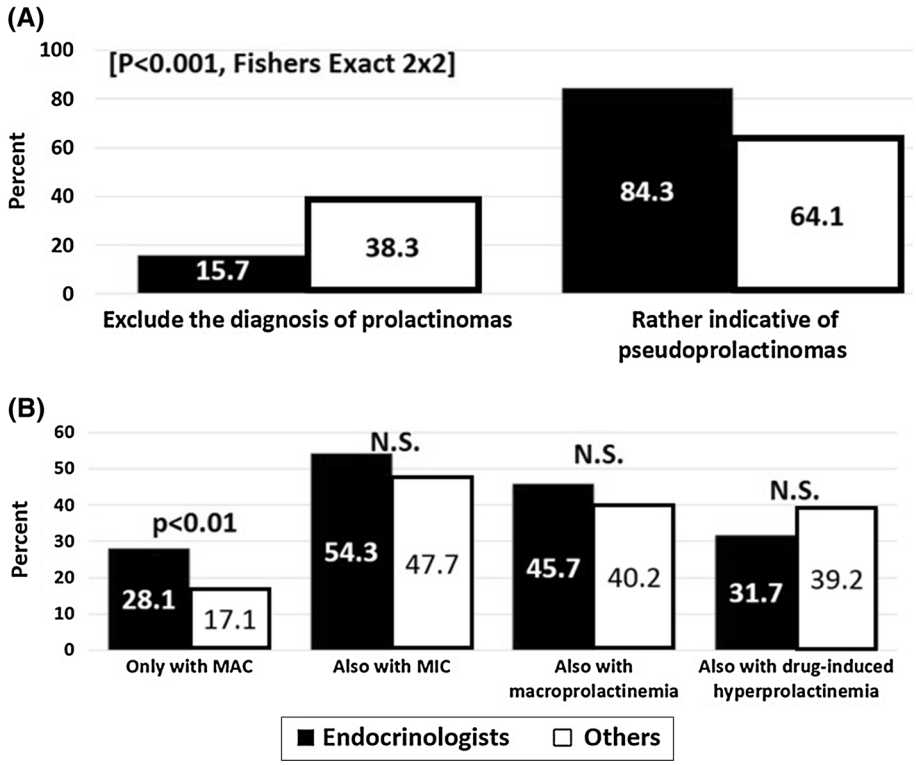

Fig. 1 **a** How would you interpret prolactin levels <100 ng/ml? **b** In which group of patients with hyperprolactinemia would you find prolactin level >250 ng/ml?

Table 3 Management approaches to microprolactinomas and macroprolactinomas by all 468 respondents together and by endocrinologists (n = 168) and non-endocrinologists (n = 298) are presented separately

Type of prolactinomas and respondents' subgroups	Responses of all physicians			Responses of endocrine and non-endocrine physicians					
	MICs (%)	MACs (%)	*P* value[a]	Microprolactinomas			Macroprolactinomas		
				Endocrine (%)	Others (%)	*P* value[b]	Endocrine (%)	Others (%)	*P* value[b]
Treat all patients	28.1	84.2	0.001	40.2	21.3	0.01	93.3	78.9	0.01
Treat symptomatic patients only	71.9	15.8	0.0001	60.8	78.7	0.01	6.6	21.1	0.01
Surgery may be a primary therapy for microprolactinomas.	6.0	–	–	2.2	7.5	n.s.	NA		
Prescribed DA' indefinitely	14.8	44.0	0.0001	6.2	20.1	0.01	50.0	40.3	n.s.
Withdrawal DA's after 2–3 years of PRL normalization	75.3	46.0	0.0001	82.1	71.2	n.s.	40.2	49.6	n.s.
Withdraw DA's after menopause if PRL is normal	9.8	9.9	n.s.	11.7	8.8	n.s.	9.8	10.1	n.s.
Bromocriptine is first DA of choice	18.4	12.8	n.s.	23.7	27.1	n.s.	6.1	16.7	0.03
Cabergoline is first DA of choice	49.8	60.4	n.s.	74.4	35.6	0.0001	83.4	47.4	n.s.
No specific preference to either DA	31.8	26.8	n.s.	10.4	37.3	0.001	22.0	35.9	0.05

All results are adjusted as percentage to account for missing responses

MIC microprolactinoma, *MAC* macroprolactinoma, *DA* dopamine agonist, *PRL* prolactin

[a] *P* values using Fisher's exact test (*t*-tailed) for responses of all physicians with regard to their approaches microprolactinomas versus microprolactinomas

[b] *P* values using Fisher's exact test (*t*-tailed) for responses of endocrine versus other physicians separately for microprolactinoma and macroprolactinomas

zone would have been credentialed by the local authorities on basis of having western-type qualification and experience. Those who identified themselves as internists with interest in endocrinology would mostly be involved with diabetes care and some service commitments in general endocrinology.

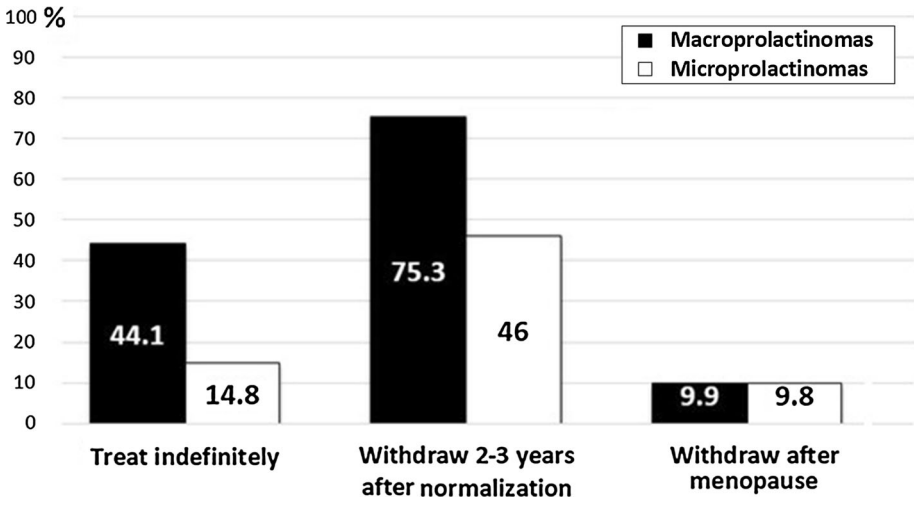

Fig. 2 Duration of treatment for microprolactinomas and macroprolactinomas

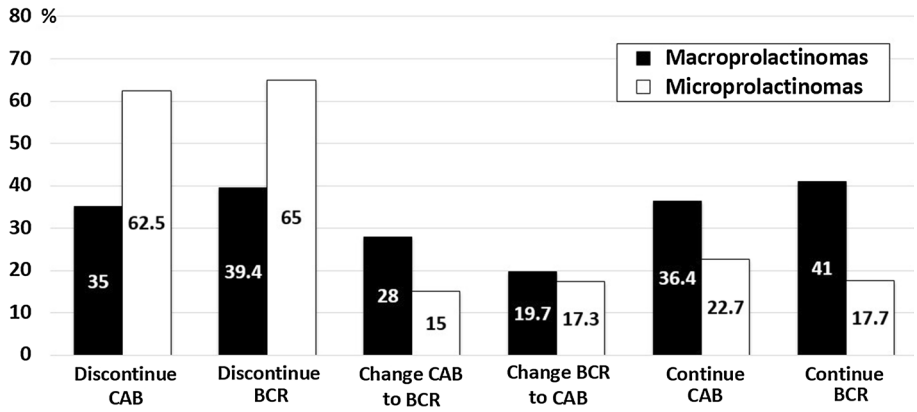

Fig. 3 Changes in dopamine agonist therapy during pregnancy

In the present study, nearly a third of respondents (16 % of endocrinologist) indicated that prolactin levels <100 ng/ml would exclude the diagnosis of prolactinomas. PRL levels usually exceed 100 ng/ml in the presence of prolactinomas, however, lower levels may be seen in cases of microprolactinomas [1–3]. Thus assuming exclusion of prolactinomas at this level will lead to missing cases. Routine screening for macroprolactin was favored by 27 % of the respondents. Although routine screening for macroprolactinemia is not the standard of practice in many pituitary centers and not endorsed by guidelines, several studies have suggested that routine screening may prevent unnecessary treatment with DAs in patients with macroprolactinemia [9].

Long-term DA therapy is well established as the first-line treatment of small prolactinomas [3–5]. Some physicians and patients however may choose surgery as primary approach because of concern over potential adverse effects or cost of long term medical therapy. Relevant systemic side effects have been reported in about one-third of patients treated with DAs, although they are generally well tolerated [10–13]. The increased risk of cardiac valve disease in patients treated with cabergoline for Parkinson's disease may have raised concerns about the safety of treatment with dopamine agonists in patients with prolactinoma although the dose range for the two conditions is markedly different [14]. Similar to recommendations by consensus guidelines, only a small percentage of our respondents recommended surgery as the first line treatment for patients with microprolactinomas. In carefully selected patients with microprolactinomas, long-term remission rates higher than 80 % have been achieved with surgery and complications from pituitary surgery for small prolactinomas are infrequent in specialized centers [15, 16].

In our survey, we found that, for patients with macroprolactinoma, 46 % of respondents favored DAs withdrawal 2–3 years after PRL normalization whereas 44 % recommended to maintain treatment indefinitely. The corresponding figures for patients with microprolactinoma were 75 and 15 %, respectively. Discontinuation of treatment 2–3 years after the achievement of normal PRL levels was recommended by 40 % of endocrinologists for patients with macroprolactinomas and by 82 % for subjects with microprolactinomas. It is well established that not all patients with

Table 4 Management approaches to microprolactinomas and macroprolactinomas by endocrinologists only from the MENA region reported in the present study and all endocrinologists from the Brazilian survey

Survey issues	MENA (%)	Brazil (%)	*P* value[a]
1. Diagnostic evaluation			
PRL level <100 ng/ml excludes the diagnosis of prolactinomas	16	38	<0.01
PRL level <100 ng/ml is indicative "pseudoprolactinomas"	84	77	
PRL levels >250 ng/ml are exclusively found in MAC	28	35	n.s.
Routine screening from macroprolactinemia	27	26	n.s.
2. Treatment decisions			
Indication for treatment of MIC: all patients	40	75	<0.01
Indication for treatment of MIC: only symptomatic patients	61	25	
Indication for treatment of MAC: all patients	93	100	<0.01
Indication for treatment of MAC: only symptomatic patients	7	0	
Surgery as primary therapy for MIC	2	7	n.s.
3. Duration of treatment			
Drugs prescribed indefinitely for MIC	6	48	<0.01
Withdrawal DA's after 2–3 years of PR normalization in MIC	82	34	
Withdraw DA's after menopause if PRL is normal: MIC	12	18	
Drugs prescribed indefinitely for MAC	50	70	<0.01
Withdrawal DA's after 2–3 years of PR normalization in MAC	40	20	
Withdraw DA's after menopause if PRL is normal: MAC	10	10	
4. The DA of choice in general			
BCR as drug of choice for MIC	24	48	<0.01
CAB as drug of choice for MIC	74	52	
BCR as drug of choice for MAC	6	30	<0.01
CAB as drug of choice for MAC	83	70	
5. The ideal DA in women planning pregnancy			
Bromocriptine	55	74	n.s.
Cabergoline	22	26	
6. Management during pregnancy			
Drug discontinuation in case of pregnancy with MIC	64	70	<0.05
Drug discontinuation in case of pregnancy with MAC	37	58	<0.01
7. Breast feeding with prolactinoma			
Allow breast feeding for all (MICs and MACs)	50	36	<0.01
Allow breast feeding with MICs only	30	44	
Breast-feeding is contraindicated in all prolactinomas	20	20	

The Brazilian data is derived from Ref. [8]

MIC microprolactinoma, *MAC* macroprolactinoma, *DA* dopamine agonist, *PRL* prolactin

[a] *P* values using Fisher's exact test 2 × 2 (*t*-tailed) or Chi square (two tailed) for responses of all Brazilian endocrinologists (721) versus MENA endocrinologists (168)

microprolactinomas need treatment [17–19]. 84 % of our respondents recommended to treat all cases of macroprolactinomas whereas 72 % of them would treat all patients with microprolactinomas. Recommendation made by endocrinologists were more discriminatory, though this has also fallen short of meeting contemporary recommendations [4, 5]. Cabergoline was favored over bromocriptine particularly by endocrinologists as the drug of choice to treat both macro- and microprolactinomas. This is along with the Endocrine Society recommendations [5] and in line with findings of the large comparative studies of cabergoline and bromocriptine convincingly demonstrating the superiority of cabergoline in terms of patient tolerability and convenience, reduction in prolactin levels, restoration of gonadal function, and tumor shrinkage [12–14]. There is no universally accepted consensus on the duration of therapy nor its therapeutic interruption after the menopause [20, 21]. Our respondents reflected these differences of practices in their responses. However, contemporary guidelines advocate that, if the patient achieves normal prolactin levels after being treated with DAs for at least 3 years

and the tumor volume is markedly reduced, a trial of tapering and discontinuation of these drugs may be initiated [3, 5].

There is now a considerable experience with the use of DAs including bromocriptine and cabergoline in patients who desire pregnancy and during pregnancy. Incidence of abortions, ectopic pregnancies or congenital malformations is not higher in infants born to mothers who conceived while taking bromocriptine and cabergoline before and during pregnancy [22]. However, the number of pregnancies studied using bromocriptine is still far exceeding that for cabergoline, accordingly, more respondents in our study favored the use of bromocriptine as the drug of choice for women with prolactinomas who wish to become pregnant although cost and availability in the region may have had some impact. Clinical practice guidelines [4, 5] and expert opinion [22] advocate that DAs should be discontinued once pregnancy has been confirmed. Reintroduction of bromocriptine if there is evidence of tumor enlargement during pregnancy is justified [22]. Among our survey respondents, 62–65 and 35–39 % advised DA withdrawal after the confirmation of pregnancy in cases of microprolactinomas and macroprolactinomas respectively. The corresponding figures for endocrinologists seemed closer to the guidelines. Women in this region are sixfold more reproductive than other regions. Patient reproductive choices may determine some of the interesting response differences seen. More patients may prefer safety and affordability when choosing medications. However, the survey was limited to a descriptive account of practice patterns without getting further details.

Finally, although nearly half of the respondents in general favored breastfeeding for women with prolactinomas and less than one-third restrict it for those with microprolactinomas. One quarter would deem it completely contraindicated; compared to 20 % of the Brazilian respondents [8]. The response was not much different among endocrinologists. There is no evidence that breastfeeding presents any risk to tumor enlargement greater than the estrogen impact of pregnancy. Breast-feeding should be allowed in these patients except for those who demonstrate signs of tumor enlargement during pregnancy requiring intervention. Three recent reviews suggested that breastfeeding does not need to be restricted. Dopamine agonists cannot be used until desired breastfeeding has been completed [22].

Although the study finding are focused on practice in the MENA region, it may have some important global implications for endocrine training based on the differences observed between the seminal study from Brazil and this paper as well as importantly unknown other potential differences which could be apparent in other regions (Africa, Eastern Europe and Asia). Although only endocrinologists' subgroup only was used to compare the present study to the findings of the Brazilian study, still several differences were detected. It is probably timely that similar well written surveys are constructed against guidelines to ascertain the quality of care, evaluate physicians' perceptions, and practices in various parts of the world. The surveys that addressed multiple aspects of thyroid disease can be taken as a model. In addition, prolactinomas being the commonest pituitary tumors should be given more prominence in international and regional professional meetings.

The study is inherently limited by its design (i.e. a survey of knowledge, attitudes and self-reported practices) rather than truly auditing the real practices and outcome. The percentage of respondents among different specialties and countries were not similar in the MENA region. Lack of a single body or association that includes all practicing endocrinologists in the MENA region make it difficult to recruit a homogeneous uniformly credentialed group of recipients and make it difficult to calculate a response rate. However, the fair sample size compared with similar studies provides some reassurance of the validity of the findings.

In conclusion, the present study documented for the first time the patterns of clinical management of prolactinomas by relevant specialties from the MENA region. It demonstrated several points of differences from contemporary guidelines regarding the diagnosis and treatment as well as management during pregnancy and postpartum. Some therapeutic approaches differed from contemporary professional guidelines. These findings should be useful in informing regional interdisciplinary discussions, focusing the needs of continuous professional developments activities, and forming the basis for future studies for monitoring clinical practice in management of this important and relatively common pituitary disorder. Prolactinomas being the commonest variety of pituitary tumors should feature more prominently in endocrine educational activities and be subject of further quality assurance exercise. Patients' access to an experienced endocrinologist who is capable of weighing the risks and benefits of various options is very important to secure comprehensive assessment and sound individualized care plan based on clinical practice guidelines. In addition, it is strongly advocated to establish "neuroendocrine multidisciplinary teams" in all centers of excellence to share experience and agree management plans particularly for difficult cases.

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Authors' contribution SAB adapted and conducted the electronic aspects of the survey. All others contributed to the manuscript and approved its final version.

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Compliance with ethical standards

Conflict of interest Salem A. Beshyah has received research grants from Novo Nordisk, Eli Lilly, Sanofi and Merck (MSD) and has received speaker's honoraria from Novartis, Servier, Abbotts, Merck Serono and Boehringer Ingelheim for subjects unrelated to this research. Ibrahim H. Sherif , Farida Chentli, Amir Hamrahian, Aly B. Khalil, Hussein Raef, Mohamed El-Fikki and Selim Jambart declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors. All participants provided an informed explicit consent to participate electronically before they proceed to participation in the survey. All data are collected anonymously.

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